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To: HV2b@NIH.gov  
Subject: Meeting with Francis  
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Harold-

I know that you are busy with your advisory council today. Indeed I will see you there this afternoon. I wanted to write down a few things to think about that came from a meeting I had with Francis Collins yesterday.

Francis recounted the discussions at Airlie house, about which you must already know:

His bottom line was that the genome project ought to speed up and that whole genome shotgun sequencing ought to be added to a geared up version of the current approach. He also made it clear that the genome community recognized that questions would be raised about the opportunity costs of ramping up the project by \$100 million over several years, which Francis thought would be necessary. Ergo he was coming to get support. In response to my questions he said there was a lot of talk at Airlie about the need to be more responsive to the needs of the broader biology community.

Over the past few weeks- probably like all IC directors- I have been getting questions about the relative value of the effort. Although clearly overstated and even naive, there was enough of a grain of truth in the Haseltine caricature in the NYT to get a lot of people asking questions.

I suggested- and Francis said that he had already come to a similar conclusion- that gene rich regions of the genome be sequenced first-- however they might be identified. This would have the advantage of putting gene sequences in the public domain more rapidly, and may diminish the most negative aspect of the Ventapillar project, i.e., the intellectual property issue. This general sentiment I hear and share for going after genes as best we can is not unlike the mouse chromosome C concept.

I this light I suggested some coordination between the genome project and CGAP, BMAP, and a similar project beginning in NIDDK (I think DMAP). Francis suggested that he Rick Klausner, and I try to set up a meeting for September to do this, but I think it might be good to think about doing this sooner.

BMAP could focus on human gene discovery first, e.g., focusing on libraries from sources such as developing human brain- something that can be does in the current federal administration, but may not always be possible. We

might then think of a smooth way of using the existing EST collections plus novel ESTs from BMAP, CGAP, DMAP to identify BACs that might receive priority treatment from the genome project- or some process like that. This might also permit increased funds for genome research (if there are to be any) to be spread across many ICs although obviously much would have to go to NHGRI. Whether or not BMAP, CGAP, DMAP, and subsequent gene discovery and mapping projects eventually feed into selecting input materials for the genome project, it would be good to coordinate them anyway.

Francis also suggested that large regions identified in human genetic studies as potentially important for disease might also be prioritized for sequencing using a process like the one that has worked so well at CIDR. I wholeheartedly endorse this.

Bottom line- I think we will effectively maintain support for the genome effort and even enhance it, only if the the existing approach fundamentally takes into account the needs and opportunities of the broader NIH community, even at the expense of increasing the administrative burden.

Steve

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